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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/727,399

12/03/2003

Liquan Luo

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EXAMINER

BERTOGLIO, VALARIE E

ART UNIT

PAPER NUMBER

1632

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DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**Office Action Summary**

Application No.

10/727,399

Applicant(s)

LUO ET AL.

Examiner

Valarie Bertoglio

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on 11/22/06;05/05/07.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☐ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) 8-25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 26-30 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12/03/2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application
- ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

This application has been transferred to Examiner Valarie Bertoglio, AU 1632.

Applicant's reply dated 02/05/2007 has been received. Claims 1-7 have been amended. Claims 26-30 have been added. Claims 8-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on August 19, 2006. Claims 1-30 are pending and claims 1-7 and 26-30 are under consideration in the instant office action. Applicant's Remarks filed 11-22-2006 are considered as well.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

#### ***Claim Objections***

Claims 1, 26 and 29 are objected to because of the following informalities: It appears claims 1, 26 and 29 may be in error in the second 'wherein' clause of claims 1 and 26 and the third 'wherein' clause of claim 29. It states that the first X-segregated progeny comprises the first chromosome and a recombined variant of the second chromosome comprising a sequence encoding the first marker. According to Figure 1, the cell comprising the first chromosome also comprises a recombined marker 2. The same mistake appears to have been made for the second progeny cell where the claim recites the recombined variant encodes the second marker, however, the figure depicts marker 1. It is noted that the second promoter appears to remain operably linked to the N terminal of the second marker; however, this is not what is

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represented by the claims. This potential discrepancy holds true for the 4<sup>th</sup> 'wherein' clause as well. Appropriate correction is required.

Claim 29 is objected to because of the following informalities:

The phrase beginning at line 3 is not consistently structured within itself. There is an (a) without a (b) and it lacks language that distinguishes the first chromosome of the pair from the second. The colon at line 4 should be replaced with a comma. The '(a)' should be deleted. The colon at line 8 should be deleted. If Applicant prefers to distinguish the chromosomes by use of (a) and (b), then (a) should be placed between "that comprises" and "in a first chromosome pair" in line 4. Like wise, (b) should be placed between " the recombinase and" and "at a homologous" at line 7.

***Claim Rejections - 35 USC § 112-1<sup>st</sup> paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Newly added claims 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed method using a first mouse whose genome comprises a transgene comprising a promoter operably linked to a gene encoding a site-specific recombinase, does not reasonably provide enablement for the claimed method wherein the first mouse comprises a transgene wherein the transgene is not stably incorporated into the genome of the mouse or wherein the transgene does not comprise a promoter operably linked to the gene encoding a recombinase or wherein the recombinase is not a site-specific recombinase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

Claims 29 and 30 are drawn to mating a second mouse having marked FRT chromosomes with a first mouse having a transgene encoding recombinase that will act on the marked chromosomes of resulting progeny. The claims do not require certain aspects for the transgene of the first mouse that are necessary to carry out such a mating. The claims fail to require that the transgene be incorporated in to the genome of the first mouse. Without such a requirement, the recombinase-encoding transgene would not necessarily be passed on to progeny of the claimed mating. Furthermore, the claim fails to require operable linkage of a promoter to the gene encoding a recombinase. Without such operable linkage, the recombinase gene would not be expressed. Without such expression, recombination would not occur. One of skill in the art would not know how to use such a method where recombination does not occur. The claim should be amended to require that the first mouse be a mouse whose genome comprises a transgene comprises a promoter operably linked to a gene encoding a site-specific recombinase.

The claims also encompass use of any recombinase, including those which are not site-specific recombinases, such as Rec proteins. The specification teaches site-specific recombination at the recombinase recognition sites on homologous chromosomes. A recombinase other than a site-specific recombinase would not be effective in carrying out the claimed method. Thus, the claims should be limited to a gene encoding a site-specific recombinase (Cre, FLP).

***Claim Rejections - 35 USC § 112-2<sup>nd</sup> paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 remain rejected and newly added claims 26-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant has amended claim 1, however, the following issue remains. Claim 1 remains unclear to the extent that it cannot be determined by the use of the word “promotes” at line 11, whether the recombination is actually required to have occurred in the mouse or whether the mere possibility or potential exists and no recombination is actually required to have taken place in the mouse. Claims 2-7 depend from claim 1.

Newly added claims 26 and 29, likewise, are unclear to the extent that it cannot be determined by the use of the word “promotes” at line 10 (claim 26) or line 12 (claim 29), whether the recombination is actually required to have occurred in the mouse or whether the mere possibility or potential exists and no recombination is actually required to have taken place in the mouse. Claims 27-28 depend from claim 26. Claim 30 depends from claim 29.

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The rejections specific to claims 5-7 are withdrawn in light of Applicant's amendments to the claims.

***Claim Rejections - 35 USC~ 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1, 2, 5, 6 under 35 U.S.C. 102(b) as being anticipated by Mao et al. (Blood 97(1):324-326, January 2001) is withdrawn in light of Applicant's arguments. Mao does not teach elements of a and b of the claim such that the required segregation would result. The structural limitations of the claim, when given the broadest reasonable interpretation of the term "marker" may be met by Mao, however, the structure of Mao would not result in the claimed segregation properties.

The rejection of claims 1, 2, 5, 6 under 35 U.S.C. 102(b) as being anticipated by Kawamoto et al. (FEBS 470:263-268, 2000) is withdrawn in light of Applicant's arguments. Kawamoto et al. does not teach elements of a and b of the claim such that the required segregation would result. The structural limitations of the claim, when given the broadest reasonable interpretation of the term "marker" may be met by Kawamoto et al., however, the structure of Kawamoto et al. would not result in the claimed segregation properties.

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**Conclusion**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Valarie Bertoglio  
Primary Examiner  
Art Unit 1632